

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/CH2004/000584

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D405/04 C07H15/00 C07D205/08

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D C07H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MUKERJEE A K ET AL: "RAPID SYNTHESIS OF DEHYDROPEPTIDES CARRYING A BETA-LACTAM MOIETY" JOURNAL OF CHEMICAL RESEARCH. SYNOPSES, LONDON, GB, no. 7, 1993, pages 280-281, XP009027094 ISSN: 0308-2342 the whole document ----- -/--	1-3,7-9



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \* & \* document member of the same patent family

Date of the actual completion of the international search

28 October 2004

Date of mailing of the international search report

08/11/2004

Name and mailing address of the ISA

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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	VAN HECK, MARGARET ET AL: "In vivo metabolism-based discovery of a potent cholesterol absorption inhibitor, SCH58235, in the rat and rhesus monkey through the identification of the active metabolites of SCH48461" JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS (1997), 283(1), 157-163, 1997, XP002275919 figure 1	1-3, 7-9, 13-17
X	----- WU, GEORGE GUANGZHONG: "A Concise Asymmetric Synthesis of A.beta.-Lactam-Based Cholesterol Absorption Inhibitor" ORGANIC PROCESS RESEARCH & DEVELOPMENT (2000), 4(4), 298-300, 2000, XP002275920 the whole document	1-3, 7-9, 13-17
X	----- UDUPI, R.H. ET AL: "Synthesis of 1-(2-carboxy-5-nitrophenyl)-3,4-substitute d azetidin-2-ones as antiinflammatory and antimicrobial agents" INDIAN JOURNAL OF HETEROCYCLIC CHEMISTRY (1996), 6(2), 99-102, 1996, XP009027043 the whole document	1-3
X	----- CLADER, JOHN W. ET AL: "2-Azetidinone Cholesterol Absorption Inhibitors: Structure-Activity Relationships on the Heterocyclic Nucleus" JOURNAL OF MEDICINAL CHEMISTRY (1996), 39(19), 3684-3693, 1996, XP002275922 the whole document	1-3, 7-9, 13-17
X	----- OTTO H-H ET AL: "STEREOCHEMIE DER DEHYDRATISIERUNG UND HALOGENIERUNG DER ALPHAR- UND ALPHAS-ISOMERE VON 3-(ALPHA-HYDROXYBENZYL)-1,4-DIPHENYL-2-AZETIDINONEN STEREOCHEMISTRY OF DEHYDRATION AND HALOGENATION OF ALPHAR AND ALPHAS ISOMERIC 3-(ALPHA-HYDROXYBENZYL)-1,4-DIPHENYL" LIEBIGS ANNALEN DER CHEMIE, VERLAG CHEMIE GMBH. WEINHEIM, DE, no. 7, 1983, pages 1162-1168, XP001179959 ISSN: 0170-2041 the whole document	1-3, 7-9
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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BROWNE, MARGARET ET AL: "Trans diastereoselective synthesis of 3-alkyl substituted.β.-lactams via the acid chloride-imine reaction of nonactivated acid chlorides" TETRAHEDRON LETTERS (1995), 36(15), 2555-8, 1995, XP004028248 the whole document	1-3,7-9, 13-17
X	BOSE, AJAY K. ET AL: "Studies on lactams. 101. Microwave-assisted rapid synthesis of.α.-amino-.β.-lactams" TETRAHEDRON LETTERS (1996), 37(39), 6989-6992, 1996, XP004030806 the whole document	1-3,7-9
X	VAN LEUSEN, ALBERT M. ET AL: "Chemistry of sulfonylmethyl isocyanides. 12. Base-induced cycloaddition of sulfonylmethyl isocyanides to carbon,nitrogen double bonds. Synthesis of 1,5-disubstituted and 1,4,5-trisubstituted imidazoles from aldimines and imidoyl chlorides" JOURNAL OF ORGANIC CHEMISTRY (1977), 42(7), 1153-9, 1977, XP002275923 the whole document	1-3,7,9
X	BURNETT, DUANE A. ET AL: "Synthesis of 3-(1-hydroxyethyl)-2-azetidinones via ester-imine condensations" JOURNAL OF ORGANIC CHEMISTRY (1985), 50(25), 5120-3, 1985, XP002275924 the whole document	1-3,7-9
X	BURNETT, DUANE A. ET AL: "2-Azetidinones as Inhibitors of Cholesterol Absorption" JOURNAL OF MEDICINAL CHEMISTRY (1994), 37(12), 1733-6, 1994, XP002275925 the whole document	1,2,5-10
X	ROSENBLUM, STUART B. ET AL: "Synthesis of 3-arylpropenyl, 3-arylpropynyl and 3-arylpropyl 2-azetidinones as cholesterol absorption inhibitors: application of the palladium-catalyzed arylation of alkenes and alkynes" TETRAHEDRON (2000), 56(31), 5735-5742, 2000, XP004213804 the whole document	1-3,7-9, 13-17

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KIRKUP M P ET AL: "(-)-SCH 57939: synthesis and pharmacological properties of a potent, metabolically stable cholesterol absorption inhibitor" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 6, no. 17, 3 September 1996 (1996-09-03), pages 2069-2072, XP004135657 ISSN: 0960-894X the whole document	1-3,7-9, 13-17
X	OTTO H-H ET AL: "DARSTELLUNG UND STEREOCHEMIE VON 3-(ALPHA-HYDROXYBENZYL)-1,4-DIPHENYL-2-AZETIDINONEN SYNTHESIS AND STEREOCHEMISTRY OF 3-(ALPHA-HYDROXYBENZYL)-1,4-DIPHENYL-2-AZETIDINONES" LIEBIGS ANNALEN DER CHEMIE, VERLAG CHEMIE GMBH. WEINHEIM, DE, 1983, pages 1152-1161, XP001012817 ISSN: 0170-2041 the whole document	1-3,7-9
X	ROSENBLUM, STUART B. ET AL: "Discovery of 1-(4-Fluorophenyl)-(3R)-'3-(4-fluorophenyl)-(3S)-hydroxypropyl)-(4S)-(4-hydroxyphenyl)-2-azetidinone (SCH 58235): A Designed, Potent, Orally Active Inhibitor of Cholesterol Absorption" JOURNAL OF MEDICINAL CHEMISTRY (1998), 41(6), 973-980, 1998, XP002275926 the whole document	1-3,7-9, 13-17
X	BURNETT, DUANE A. ET AL: "Synthesis of fluorescent biochemical tools related to the 2-azetidinone class of cholesterol absorption inhibitors" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS (2002), 12(3), 315-318, 2002, XP002275927 the whole document	1-3,7-9, 13-17
X	BURNETT, DUANE A. ET AL: "Synthesis of iodinated biochemical tools related to the 2-azetidinone class of cholesterol absorption inhibitors" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS (2002), 12(3), 311-314, 2002, XP002275928 the whole document	1-3,7-9, 13-17
X	US 5 631 365 A (ROSENBLUM STUART B) 20 May 1997 (1997-05-20) the whole document	1-3,7-9, 13-17
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 524 595 A (SCHERING CORP) 27 January 1993 (1993-01-27) the whole document	1-3,7-9, 13-17
X	WO 00/63703 A (SCHERING CORP) 26 October 2000 (2000-10-26) the whole document	1-3,7-9, 13-17
X	US 5 633 246 A (DUGAR SUNDEEP ET AL) 27 May 1997 (1997-05-27) the whole document	1-3,7-9, 13-17
X	WO 02/50090 A (SCHERING CORP) 27 June 2002 (2002-06-27) the whole document	1-3,7-9, 13-17
X	DE 36 20 467 A (CIBA GEIGY AG) 2 January 1987 (1987-01-02) the whole document	1-3,7-9, 13-17
X	WO 03/026643 A (SCHERING CORP) 3 April 2003 (2003-04-03) * the whole document, in particular page 42 formula X, XI *	1-3,7-9, 13-17
X	US 5 756 470 A (VAN HECK MARGARET ET AL) 26 May 1998 (1998-05-26) the whole document	1-17
X	WO 97/16455 A (SCHERING CORP) 9 May 1997 (1997-05-09) the whole document	1-17
X	US 2003/119428 A1 (DAVIS HARRY R ET AL) 26 June 2003 (2003-06-26) the whole document	1-17

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### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-7, 9-17  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

Continuation of Box II.2

Claims Nos.: 1-7, 9-17

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty or inventive step. So many documents were retrieved that it is impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT).

Furthermore, present claims 1-7, 9-17 relate to an extremely large number of possible compounds. In fact, the claims contain so many options, variables or possible permutations that a lack of clarity (and conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and concise), namely claim 8.

Nevertheless, most of the references cited are also relevant to the subject-matter of claims 1-7, 9-17.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

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